REMARKS

The Office Action mailed August 27, 2002, set a three-month shortened statutory period for response expiring November 27, 2002. Pursuant to the Petition for Extension of Time under 37 C.F.R. 1.136(a) submitted herewith, the period for reply is extended three months to February 27, 2003. This amendment is therefore timely filed.

Claims 1-4, 6-9, 11, 12, and 14-43 were in the application prior to the instant amendment. Claim 2 is amended herein to place it in independent form and claim 1 is cancelled without prejudice to the prosecution thereof in a continuing application. Thus, the application, as amended, contains claims 2-4, 6-9, 11, 12, and 14-43.

Claims 1-3, 6-8, 12, and 30 are rejected under 35 U.S.C. § 102(b) as being anticipated by Penners et al, U.S. Patent No. 5,651,985 on the grounds that the patent teaches a pharmaceutical dosage form designed to have an extended gastric residence time in order to increase the amount of an active substance absorbed in the upper gastrointestinal tract; that the dosage form comprises the active substance and customary pharmaceutical excipients, as well as a mixture of polymers containing lactam groups and polymers containing carboxyl groups; and that the dosage form may also optionally comprise a gas-generating component. The Examiner further notes that polyvinylpyrrolidone is given as an example of a polymer containing a lactam group, and carboxymethylcellulose and acrylic resins are given as examples of polymers containing carboxyl groups.

The rejection is respectfully traversed and reconsideration thereof is requested. First of all, insofar as it applies to claim 1, the rejection is moot in view of the cancellation of said claim. With respect to claim 2 and claims 3, 6-8, 12, and 30, which directly or ultimately depend from claim 2, the Examiner correctly points out that the compositions of the '985 patent contain, as gel-forming agent, a mixture of polymers containing lactam groups, such as polyvinylpyrrolidone, and polymers containing carboxyl groups, such as acrylic resins, i.e., a mixture of polymers selected from different polymer families. Applicants' claimed compositions contain a swelling hydrophilic polymer matrix which consists of a hydrophilic polymer selected from certain specified families of hydrophilic polymers, or a mixture of hydrophilic polymers selected from within the same polymer family. Applicants' claims plainly do not read on a composition

containing a polymer matrix consisting of a mixture of polymers selected from different polymer families, such as a mixture of a polyvinylpyrolidone and an acrylic acid polymer and, hence, cannot be anticipated by the '985 patent. Withdrawal of the rejection is respectfully requested.

Claims 2-4 (Claim 1 having been cancelled), 6-9, 11, 12, and 14-43 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Penners et al in view of Wong et al, U.S. Patent No. 6,120,803, Shell WO 97/47285, and Maggi et al WO 98/08515. The Examiner notes that the Penners et al patent does not teach a gastric-retentive dosage form which further comprises a hydrophilic excipient capable of promoting polymer hydration, nor does it disclose lipid substances to be used in the dosage form or that benzamides, alpha-1 antagonists, or those active substances listed in claim 27 can be used as the active ingredient in the disclosed dosage form.

The Examiner states that the Wong et al patent teaches a dosage form designed for retention in the stomach and prolonging the delivery of an active substance in that environment; that the disclosed dosage form comprises water-soluble polymers, including polyvinylpyrrolidone, hyroxypropylcellulose, hydroxypropylmethylcellulose, sodium carboxymethylcellulose, xanthan gum, and blends thereof, hydroattractant polymeric excipients, such as microcrystalline cellulose, other excipients, including mannitol, sorbitol, polaxamers, polysorbates, effervescing couples, such as citric acid blended with sodium bicarbonate, and also comprises a band made from materials such as ethylcellulose, copolymers of acrylic acid and methacrylic acid, carnuba wax, white or yellow beeswax, castor wax, and mixtures thereof; and that captopril, amoxicillin, and prazosin hydrochloride are drugs suitable for this invention.

The Shell document is purported to disclose a dosage form designed to administer a drug at a sustained rate of release for an extended period of time in the stomach and upper intestinal tract, comprising a water-swellable polymer matrix and that captopril and metoclopramide are among the drugs that would benefit from such a delivery system.

The Maggi et al reference is stated to disclose a dosage form for the controlled release of alfuzosin hydrochloride which dosage form comprises a layer that swells upon contact with aqueous biological fluids and a layer comprising the active ingredient in a hydrophilic polymer matrix, and which is designed to release the drug at the proximal

segments of the gastrointestinal tract, namely the duodenum and the jejunum.

The Examiner urges that it would be obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Penners et al, Wong et al, Shell, and Maggi et al into the objects of the instant application. Based on the similarities of their respective disclosures, one of ordinary skill would be motivated to combine the teachings of Penners et al and Wong et al because, as stated *In re Kerkhoven*, 205 USPQ 1069, 1072 (CCPA-1980), "It is *prima facie* obvious to combine two compositions, each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition which is to be used for the very same purpose." Applicants respectfully disagree.

As noted hereinabove, the Penners et al compositions require a mixture of polymers selected from different polymer families. As stated at column 7, lines 20-21 of the '985 patent, gels are only formed if both polymeric components are present. Pure PVP (a polymer containing lactam groups) is not a stable gel-forming agent. Likewise, Comparison Example 4 shows that carboxymethylcellulose and polyacrylate (polymers containing carboxyl groups) alone have poor mechanical properties, are strongly sensitive to erosion, and are deformed irreversibly even with low mechanical stress. Accordingly, Penners et al teach that a mixture of specific polymers selected from different polymer families is essential to operability, and the reference therefore actually teaches away from Applicants' compositions which require a single polymer or a mixture of polymers selected from the same polymer family.

The dosage forms disclosed by Wong et al contain a polymer matrix formed of a mixture of a swellable polymer chosen from numerous families of water-soluble polymers and a hydroattractant chosen from numerous families of water-insoluble polymers. Thus, like Penners et al, Wong et al teach the need for a mixture of different polymers not required in Applicants' compositions. Moreover, the Wong et al dosage forms require a band of rigid or semi-rigid insoluble material circumscribing a portion of the polymer matrix. No such band is required in Applicants' compositions. That Wong et al recites long lists of polymers, excipients, and active ingredients absent from the disclosure of the primary reference in compositions that are different from both those of the primary Penners et al reference and those here claimed, is simply not a teaching that

would suggest modifying the teaching of Penners et al in such a way as to arrive at Applicants' claimed compositions. Hence, Wong et al adds nothing to Penners et al.

The Shell reference discloses compositions containing a water-swellable matrix and a chemical agent that pharmacologically induces the fed mode in the patient's stomach, e.g., serotonin receptor antagonists, C_{10}-C_{15} fatty acids, L-typtophan, to achieve retention of the drug in the stomach. Applicants' claimed compositions require no such chemical agent. Clearly, nothing in the Shell reference, considered alone or in combination with Wong et al, would suggest modifying the Penners et al compositions to arrive at Applicants' compositions. Accordingly, Shell adds nothing to the primary Penners et al reference.

Maggi et al disclose multi-layer alfuzosin-containing tablets, at least one of which layers acts as a barrier to the passage of alfuzosin. Nowhere does the reference suggest a carbon dioxide generating system such as required in Applicants' compositions. Thus, like the Wong et al and Shell references, the Maggi et al reference adds nothing to the primary Penners et al reference, and considered alone or in combination with Wong et al and/or Shell contains nothing that would suggest modifying the composition of Penners et al to arrive at Applicants' compositions.

The instant rejection is based on a mosaic of four references, each of which discloses certain ingredients also contained in the instantly claimed compositions. However, all the compositions disclosed in the cited references differ from each other as well as from Applicants' compositions both in content and mode of functioning. The mere fact that individual ingredients of Applicants' compositions can be found listed in a collection of prior art references is not tantamount to a teaching of the means of assembling the ingredients so as to produce Applicants' compositions having the properties and uses described therefor. Accordingly, there is nothing in the cited references, whether considered individually or in any combination, which would have taught or suggested the compositions here-claimed. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

There being no remaining issues, this application is believed in condition for favorable reconsideration and early allowance and such actions are earnestly solicited.

Attached hereto is a marked-up version of the changes made to the claims by the instant amendment. The marked-up version is entitled "Version With Markings To Show Changes Made".

Respectfully submitted,

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Version With Markings to Show Changes Made

In the Claims:

Claim 1 has been cancelled.

Claim 2 has been amended as follows:

2. (Twice amended) A ~~composition according to Claim 1 wherein the swelling polymer matrix consists~~ controlled-release pharmaceutical composition with gastric residence comprising two or three layers and further comprising:
(a) an active principle combined with an excipient which modifies its release,
(b) a carbon dioxide-generating system in a swelling hydrophilic polymer matrix consisting of a hydrophilic polymer chosen from the following families of hydrophilic polymers:
- natural polysaccharides,
- cellulose derivatives,
- polyvinylpyrrolidones,
- polymers derived from acrylic acid and methacrylic acid and salts thereof, or
- aminoacid polymers,
or a mixture of 2 or 3 hydrophilic polymers chosen from the same family.
wherein (a) and (b) are included in the same layer [(a)+(b)] or in separate layers [(a)] and [(b)] and wherein multiple layers containing (a), (b) or (a) and (b) in the same tablet have the same or different compositions and dimensions.